15.0 AMYOTROPHIC LATERAL SCLEROSIS (ALS)

STATEMENT TO THE PUBLIC

Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's Disease)

The reviewers used two distinct sets of guidelines to evaluate the evidence:

- *Using the guidelines that the International Agency for Research on Cancer uses to assess cancer risks, they considered the evidence to warrant a "possible (2B)" cause of ALS on the basis of limited epidemiology. A work group convened by the National Institutes of Environmental Health Sciences considered the evidence "inadequate" (Group 3). The British National Radiological Protection Board noted a consistent epidemiological association with high-exposure electrical occupations but speculated that it might be due to shocks.*

- *Using Guidelines developed specifically for the California EMF Program, the DHS reviewers were all "close to the dividing line between believing and not believing" that EMFs increased the risk of ALS to some degree.*

The DHS scientists are more inclined to believe that EMF exposure increased the risk of ALS than were the majority of the members of scientific committees convened to evaluate the scientific literature by the NIEHS in 1998, and by the NRPB in 2001. There are several reasons for these differences. The three DHS scientists thought there were reasons why animal and test tube experiments might have failed to pick up a mechanism or a health problem; hence, the absence of much support from such animal and test tube studies did not reduce their confidence much or lead them to strongly distrust epidemiological evidence from statistical studies in human populations. They therefore had more faith in the quality of the epidemiological studies in human populations and hence gave more credence to them.

Lou Gehrig's Disease has a low incidence with rates around 1/100,000 a year. Even doubling such rates and accumulating them over a lifetime leaves accumulated lifetime risks less than 1/1,000. Thus the vast majority (99.9%) of highly-exposed people would still not contract this disease. Furthermore, calculations suggest that the fraction of all cases of this condition that one could attribute to EMFs would be no more than a few percent of the total cases (if any). However, if EMFs do contribute to the cause of these conditions, even the low fractions of attributable cases and the size of accumulated lifetime risk of highly exposed individuals could be of concern to regulators. Indeed, when deemed a real cause, estimated lifetime risks smaller than these (1/100,000) have triggered regulatory evaluation and, sometimes, actual regulation of chemical agents such as airborne benzene. The uncommon, accumulated high-EMF exposures implicated by the evidence about these conditions come from unusual configurations of wiring in walls, grounded plumbing, nearby power lines, and exposure from some jobs in electrical occupations. There are ways to avoid these uncommon accumulated exposures by maintaining a distance from some appliances, changes in home wiring and plumbing, and power lines. However, to put things in perspective, individual decisions about things like buying a house or choosing a jogging route should involve the consideration of certain risks, such as those from traffic, fire, flood, and crime, as well as the uncertain comparable risks from EMFs.

The EMF Program's policy analysis required each of the three DHS scientists to express in numbers their individual professional judgments that the range of added personal risks suggested by the epidemiological studies were "real." They did this as a numerical "degree of certainty" on a scale of 0 to 100. For the conditions with the most suggestive evidence of EMF risk, the three scientists each came up with a graph that depicts their best judgments with a little "x" and the margin of uncertainty with a shaded bar:

CONDITION	REVIE-WER	IARC CLASS	CERTAINTY PHRASE	IRL	DEGREE OF CERTAINTY FOR POLICY ANALYSIS THAT AN AGENT (EMFs) INCREASES DISEASE RISK TO SOME DEGREE
ALS (Lou Gehrig's Disease)					0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100
	1	2B	Close to dividing line	9	
	2	2B	Close to dividing line	21	
	3	2B	Close to dividing line	11	

15.1 EPIDEMIOLOGICAL EVIDENCE

Figure 15.1 ALS RRs

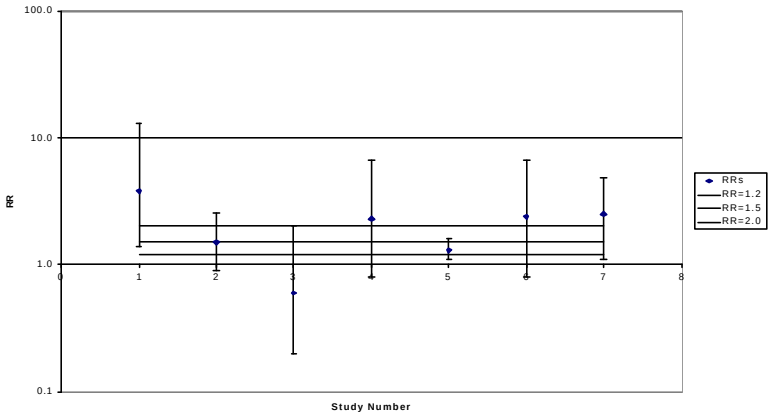

Figure 15.1 and Table 15.1 display the seven studies which deal with electrical occupation or estimated magnetic field exposure and the occurrence of amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's Disease). The graph shows the relative risks reported in the seven studies. Ahlbom (Ahlbom, 2001) calculated the meta-analytic summary relative risks for all seven, the clinic based studies, the mortality based studies and the two utility cohort studies which assigned magnetic field exposure based on a job-activity matrix. For all seven studies the meta-analytic summary RR was 1.5 (1.2-1.7). For the two utility cohort studies it was 2.7 (1.4-5.0). Thus the evidence suggests an association between ALS and working in an electric occupation, or having a job within a utility company with a high magnetic field exposure. Six of seven studies report RR above 1.0 (P=.055). Given the small number of studies, the fact that 86% of the relative risks are above 1.0 does not achieve conventional statistical significance.

TABLE 15.1.1

STUDY NUMBER	REFERENCE	STUDY POPULATION AND SUBJECT IDENTIFICATION	DEFINITION AND ESTIMATION OF EXPOSURE	STUDY DES.	NUMBERS	RESULT RR (95% C.L.)
1	(Deapen & Henderson, 1986)	Study population: not specified. Cases: ALS society, US in 1979. Controls: friends	Questionnaire: electrical occup 3 yr prior to diagnosis.	CC	678 cases (19 electr occ) 518 controls (5 electr. occ.)	3.8 1.4-13.0
2	(Gunnarsson, 1991)	Male population of Sweden 1970-83. Cases: Deaths with ALS as underlying or contributing cause in mortality registry. Controls: Random sample from population.	Job title in census 1960: electricity worker.	CC	1067 cases (32 exposed) 1005 controls	1.5 0.9-2.6
3	(Gunnarsson, 1992)	Male population of central and southern Sweden in 1990. Cases: Patients with MND in neurological departments. Controls: Random sample from population.	Questionnaire: electricity work and exposure to MF.	CC	58 cases (4 MF exposure) 189 controls	0.6 (MF exp) 0.2-2.0
4	(Davanipour et al., 1997)	Study base: not specified. Cases: ALS	Questionnaire about occupational history:	CC	28 cases	2.3

STUDY NUMBER	REFERENCE	STUDY POPULATION AND SUBJECT IDENTIFICATION	DEFINITION AND ESTIMATION OF EXPOSURE	STUDY DES.	NUMBERS	RESULT RR (95% C.L.)
		patients at outpatient clinic in southern California. Controls: relatives.	EMF exposure assessed by hygienist. Cumulative (E1) and average (E2) exposure.		32 controls cut off: 75th percentile, of case distribution	0.8-6.6 average (E2)
5	(Savitz, Loomis & Chiu-Kit, 1998b)	Male population in 25 states, US, 1985-91. Cases: deaths from ALS. Controls: Deaths from other causes.	Job title on death cert.: electrical occupation in aggregate and individual jobs.	CC	114 cases in electr. occup. in aggregate	1.3 1.1-1.6
6	(Savitz et al., 1998a)	Male employees at five US utility companies 1950-1988. Cases: deaths with ALS mentioned on death certificate, identified through multiple tracking sources.	Measurements and employment records. Combination of duration and EMF index.	Cohort	9 cases with >20 years in exposed occup.	2.4 0.8-6.7
7	(Johansen & Olsen, 1998a)	Male employees in Danish utility companies observed during 1974-1993. Cases: deaths from ALS in mortality registry.	Employment records and JEM: estimated average exposure level.	Cohort	21236 males in cohort. 14 (9 exposed) cases	2.5 1.1-4.8

15.2 ARGUMENTS FOR AND AGAINST CAUSALITY

TABLE 15.2.1

CHANCE		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Not all the associations are above 1.00 or statistically significant.	(F1) The narrow confidence limits in the meta-analytic summaries and the low likelihood of this pattern of evidence by chance leans away from chance as an explanation.	(C1) A non-chance explanation must be sought.
(A2) Each of the studies have small numbers of exposed cases.	(F2) There are 18 exposed cases in the two cohort studies and 175 “exposed” cases in the other studies.	

TABLE 15.2.2

BIAS		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) The case-control studies are subject to recall bias. All studies are subject to the authors presenting only the strongest associations of the many generated during analysis. For example in the Savitz, Checkoway (Savitz et al., 1998a) study, there was no association with ALS for durations less than 20 years and no dose response with duration of occupation.	(F1) Like the electric shock and trauma associations in questionnaire-based case control studies, electrical occupation is subject to recall bias. But two large occupational cohort studies and a case control study objectively assessing EMF exposure show a higher ALS rate and an association with high EMF work. Even if one were to discard the Savitz, Checkoway (Savitz et al., 1998a) study as gerrimandered, the Johansen (Johansen & Olsen, 1998a) study remains.	(C1) Bias upward is not a big concern in this evidentiary base. Bias downward might be a problem.
	(F2) If there is any consistent bias it is non-differential measurement error which would tend to obscure associations.	

TABLE 15.2.3

CONFOUNDING		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) One doubts that electrical occupation or high-EMF electrical work is associated with ALS. Johansen (Johansen & Olsen, 1998a) showed that fatal electric shock was associated with high-EMF jobs. Serious non-lethal shocks should be more common in high-EMF jobs also.	(F1) Since high amperage is often associated with high voltage, it is not surprising that high magnetic field jobs would have a higher probability of death among those shocked. It does not follow that the frequency of shocks would be greater.	(C1) The evidentiary base to describe the frequency of shocks and link them to EMF exposure in an objective way is non-existent, so any link between magnetic field and shock exposure is speculative.
(A2) If it is, then the association is not due to magnetic fields but to the delayed effect of many shocks experienced in those jobs. Experimental work shows that shocks, not EMF exposure is responsible for acute vascular trauma.	(F2) Kondo (Kondo & Tsubaki, 1981) and Gunnarson (Gunnarsson, 1992) showed weak protective associations with shock. The other studies (Deapen & Henderson, 1986), (Savettieri et al., 1991), (Cruz et al., 1999) were of borderline statistical significance, so by conservative criteria 5 out of 6 studies were null. Four out of 6 studies had ORs larger than 1.00.	(C2) The reported associations with ALS based on objective assessments of magnetic field are of about the same strength as those conveyed by subjectively recalled shock history in the general public.
(A3) (Kurtzke, 1980) and others have shown association between ALS and physical injury many years before. Electrical trauma may also have delayed effects.	(F3) All these studies rely on recall.	(C3) One would need to believe that virtually all high EMF electrical workers had experienced shocks which rendered them unconscious during their work life, or that common minor shocks carry the same risk as major shocks, for shocks to explain the magnetic field association with ALS. This seems implausible on the face of it but needs to be evaluated.
(A4) (Deapen & Henderson, 1986), (Gallager, 1987), (Cruz et al., 1999), and (Savettieri et al., 1991) showed associations between ALS and self reported electrical shock, often years before.	(F4) The ORs conveyed by shock leading to uncosciousness in (Deapen & Henderson, 1986) is 2.8 (1.0-9.9). The ORs conveyed by high EMF work excluding 3 out of 19 workers with shock is 3.3 (1.1-10.3) Shock to unconsciousness does not explain the EMF association. One needs to postulate that virtually all high EMF workers have received lesser shocks which conveyed more risk than shock to unconsciousness. [Cruz 1999 #1460] reports a RR	(C4) A similar concern, as voiced in C3, would apply to contact currents as a confounder of magnetic fields.

CONFOUNDING		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
	= 0.7 (0.5-1.1) from multiple non-injury shocks.	
(A5) Gunnarsson (1992) reports an association with solvent exposure RR = 15.6 (2.8-87.0). This has not been ruled out as a confounder.	(F5) Gunnarson had 58 cases and 189 controls. McGuire (McGuire et al., 1997) with 174 cases and 348 controls reports a solvent exposure RR for males of 1.3 (0.7-2.3). This is too weak to explain EMF association.	(C5) For the same reason it is also implausible that the history of physical trauma or solvent use in high-EMF workers could explain the association. The 60-year-old literature (Alexander, 1938) in shock pathology relates to acute not delayed effects.

TABLE 15.2.4

STRENGTH OF ASSOCIATION		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) The associations are modest and could be due to bias.	(F1) Associations of 2.5 and 3.0 are not so easy to dismiss by invoking bias or confounding.	(C1) We do not put much weight on bias as a default explanation without specific evidence.
		(C2) The utility study associations are not so small and are not subject to recall or selection bias.
		(C3) Exposure misclassification could lead to downward bias.

TABLE 15.2.5

CONSISTENCY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) One should only pay attention to statistically significant associations. Of 7 studies of electrical work or magnetic field exposure, only 3 were significant and the ORs ranged from 1.3 to 3.8.	(F1) One should look at the general pattern among 7 studies. Six reported ORs above 1.00.	(C1) There is a recurrent finding of relative risks moderately above the resolution power of the studies suggesting an association between electrical work and jobs with high magnetic fields and the occurrence of ALS.

TABLE 15.2.6

HOMOGENEITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Not all the associations are statistically significant.	(F1) All the studies are compatible with a RR of 1.5.	(C1) The heterogeneity in the 86% of studies with RRs above 1.0 is not great and has a reasonable explanation.
(A2) Estimates of association vary with no clear central tendency.	(F2) The small heterogeneity has a reasonable explanation. The studies with the crudest exposure had lowest RR, those with the highest propensity to selection bias had the highest RR, and the occupational studies with good exposure assessment had associations in between with pooled RR = 2.7 (1.4-5.0).	

TABLE 15.2.7

DOSE RESPONSE		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Only 3 of the 7 studies allow the reviewers to look at magnetic field exposure from job-exposure matrices.	(F1) All three studies that ranked jobs by exposure show increasing risk with EMF exposure, but confidence intervals are wide.	(C1) The evidentiary base is not voluminous and the size of the studies are not sufficient to get a clear picture of dose response, but the pattern of evidence is more what one would expect if something about high EMF jobs, held for a long time, caused ALS.
(A2) Davanipour (Davanipour et al., 1997) shows no statistically significant associations for the whole group.	(F2) When the (Johansen & Olsen, 1998a) upper two categories of exposure are combined the SMR is 2.5 (1.1-4.8).	
(A3) Johansen (Johansen & Olsen, 1998a) shows no statistically significant associations for the entire group.	(F3) For both Davanipour (Davanipour et al., 1997) and Savitz (Savitz, 1998), a stronger dose response is seen in persons who have worked for at least 20 years. The associations (high to low) are respectively 5.5 (1.3-22.5) and 2.4 (0.7-8.0).	
(A4) There is no statistically significant dose response. This should pull down confidence a lot that something about high-EMF work (much less the EMF mixture itself) causes ALS.	(F4) In Savitz (Savitz et al., 1998a), only the 20-year exposure group displayed associations with narrow confidence limits. The other durations of occupation displayed associations with wide confidence limits and with no obvious pattern.	
(A5) Savitz (Savitz et al., 1998a) reports only the results for greater than 20 years exposure, the 10-20 year group shows some protection from EMF exposure.		

TABLE 15.2.8

COHERENCE/VISIBILITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Electricity is everywhere. Why have we not seen an obvious epidemic of ALS?	(F1) Both exposures to strong EMF and ALS are rare events. The rate of ALS in the highly exposed group is only a few cases per hundred thousand.	(C1) If real, this would take sophisticated studies to detect and would not be obvious.

TABLE 15.2.9

EXPERIMENTAL EVIDENCE		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
No evidentiary base.	No evidentiary base.	(C1) There are no EMF animal bioassays for ALS.
		(C2) Experiments showing bioeffects at high EMF levels increases somewhat the credibility of EMF effects in general.

TABLE 15.2.10

PLAUSIBILITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) There is no known physical induction mechanism nor a chain of mechanisms leading from exposure to pathology.	(F1) It takes a while to figure out the causal processes underlying observations.	(C1) The lack of a mechanism does not pull confidence down as much as the presence would pull it up.

TABLE 15.2.11

ANALOGY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
See "Generic Issues" chapter.		

TABLE 15.2.12

TEMPORALITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
See "Generic Issues" chapter.		

TABLE 15.2.13

SPECIFICITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
See "Generic Issues" chapter.		

TABLE 15.2.14

OTHER DISEASE ASSOCIATIONS		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) No mechanistic reason to pay attention to associations with other diseases.	(F1) Association with Alzheimer's, depression/suicide, and arrhythmic death suggest neurological effects. (F2) Association with other diseases strengthens confidence in EMF mixture bioeffects.	(C1) Has some relevance.

TABLE 15.2.15

SUMMARY TABLE FOR ALS			
	HOW LIKELY IS THIS ATTRIBUTE OF THE EVIDENCE UNDER:		
ATTRIBUTE OF THE EVIDENCE	**"NO-EFFECT" HYPOTHESIS**	**CAUSAL HYPOTHESIS**	**HOW MUCH AND IN WHAT DIRECTION DOES THIS ATTRIBUTE CHANGE CERTAINTY?**
Chance highly unlikely according to meta-analysis.	Unlikely		A non-chance explanation is needed
Upward bias not suggested. Cohort studies most likely free of bias report RR of 2.7 (1.4-5.0).	Unlikely	Possible	Slight increase
Confounding by shocks proposed but not highly credible.	More Possible	Possible	No impact or slight decrease
Combined bias, confounding, and chance.	Possible	Possible	Slight decrease
Strength of association does not fully exceed plausible bias or confounding.	More Possible	Possible	No impact or slight decrease
Consistency of association: 86% of RR above 1.0 (probability = 0.055).	Unlikely	Possible	Some increase
Dose response suggestive but not clear.	Possible	More possible	No impact or slight increase
Coherent with national and temporal trend.	Possible	Possible	No impact
Experimental: No EMF bioasays.	NA	NA	No impact
Plausibility: No mechanistic explanation.	Possible	Possible	No impact
No analogy.	Possible	Possible	No impact
Temporality.	NA	NA	No impact
Specificity: effect not restricted to subtype, other disease associations.	Possible	Possible	No impact, slight increase

15.3 Posterior (Updated) Degree of Certainty and IARC Classification

15.3.1 Statements of Individual Reviewers

Reviewer 1 (DelPizzo)

Degree of Certainty: The epidemiological studies present a fairly consistent pattern, with 6 out of 7 studies reporting RR > 1. The meta-analysis suggests that these results are not due to chance. It is this reviewer's judgment that the results are not likely to be due to bias or confounding, given the diversity of the studies' populations and design. The credibility of the hypothesis of hazard is boosted by the high degree of certainty attributed to other associations and the weakness of the arguments for an alternative explanation. In this reviewer's judgement, an appropriate evaluation is "close to the dividing line between believing and not believing" that EMFs increase the risk of ALS to some degree. For decision analysis purposes, the reviewer would use values between 20 and 80, with a median of 55.

IARC Classification: 2B, possible human hazard.

Reviewer 2 (Neutra)

Degree of Certainty: An association somewhat above the resolution power of the studies that shows up with moderate consistency in studies with and without the likelihood of upward bias and without an obvious confounder pulls up one's initial degree of certainty quite a bit despite the lack of analogous agents and a biological explanation. To give credence to the possibility of shocks or contact currents as the true agent to explain this association requires that the association with magnetic field exposure be quite strong and that these shocks be known to produce a larger association with ALS than magnetic fields do. The evidence for either of these assertions is weak to absent. This reviewer would characterize degree of certainty as "close to the dividing line between believing and not believing" that EMFs increase the risk of ALS to some degree. For the purposes of the decision model, a median degree of certainty of 52 ranging from 20 to 65.

IARC Classification: An IARC Classification of "Possible 2B" would be warranted by the fairly consistent epidemiological studies, tempered by the residual uncertainty as to whether magnetic fields are the responsible agent, and the lack of animal models or mechanistic explanations of the phenomenon. One could argue that the two utility cohort studies provide confirmation of the Deapen (Deapen & Henderson, 1986) and Davanipour (Davanipour et al., 1997) and Savitz death certificate study (1998a) that something about electrical occupations conveys risk, much in the way that IARC sometimes lists occupation in an industry as a cause for cancer and that the occupation (as opposed to magnetic fields in the occupations) warrants a 2A classification on the basis of consistent epidemiological evidence in humans.

Reviewer 3 (Lee)

Degree of Certainty: The human evidence of the ALS studies is based on seven occupational studies that differ considerably in design. This reviewer's posterior is increased over the prior due to the consistent associations mostly above a RR of 1.0. However, the posterior is slightly decreased for a lack of a dose response and the fact that confounding and bias cannot be ruled out. Hence, the posterior degree of certainty for purposes of the policy analysis falls within the "close to the dividing line between believing and not believing" that EMFs increase the risk of ALS to some degree category with median of 55 and a range of 20 to 75.

IARC Classification: The human evidence is modest but not consistent with chance explaining the body of evidence. Bias and confounding cannot be ruled out. Also, the animal evidence is inadequate, and there is no sound mechanistic rationale. Nonetheless, the evidence as a whole is sufficient for a Group 2B "possible human hazard."

15.3.2 SUMMARY OF THE THREE REVIEWERS' CLASSIFICATIONS

CONDITION	REVIE-WER	IARC CLASS	CERTAINTY PHRASE	IRL	DEGREE OF CERTAINTY FOR POLICY ANALYSIS THAT AN AGENT (EMFS) INCREASES DISEASE RISK TO SOME DEGREE
ALS (Lou Gehrig's Disease)					0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100
	1	2B	Close to dividing line	9	
	2	2B	Close to dividing line	21	
	3	2B	Close to dividing line	11	

15.4 QUESTIONS RELEVANT TO DOSE RESPONSE AND POLICY

TABLE 15.4.1

HOW CONFIDENT ARE THE REVIEWERS THAT SPECIFIC EXPOSURE METRIC OR ASPECT OTHER THAN 60 HZ TWA MAGNETIC FIELD IS ASSOCIATED WITH THIS DISEASE?	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
No evidentiary base.	No impact.

TABLE 15.4.2

EVIDENCE FOR THRESHOLD OR PLATEAU	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) Davanipour (Davanipour et al., 1997) and Savitz (Savitz et al., 1998a) show an upward trend in risks with microtesla-years with no threshold or plateau in those with 20+ years of work. Johansen (Johansen & Olsen, 1998) shows the same for all workers. (C2) Only 3 studies are relevant. No suggestion of threshold or plateau.	(I1) Cannot provide "safe" dose or much dose-response information.

TABLE 15.4.3

EVIDENCE FOR BIOLOGICAL WINDOWS OF VULNERABILITY	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
No evidentiary base. Primarily daytime long-term exposure.	None.

TABLE 15.4.4

CONSISTENT INDUCTION PERIOD OR REQUIRED DURATION OF EXPOSURE	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) To the extent there is any evidence (Savitz and Davanipour), it suggests an interval between exposure and disease around 20 years, the kind of interval seen in studies of the delayed effect of trauma and not the shorter intervals claimed for cancer induction in EMFs. (C2) Not all disease processes initiated by EMFs would have the same induction period.	None.

TABLE 15.4.5

EMFs COMPARED TO OTHER RISK FACTORS FOR THIS DISEASE	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) Similar to other reported associations (McGuire et al., 1997) as to size and frequency of occurrence. Not really relevant in any case.	None.

TABLE 15.4.6

RELATIVE RISK COMPARED TO THAT WHICH WOULD GENERATE 1/1,000 OR 1/100,000 THEORETICAL LIFETIME RISK	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) With annual mortality of 1/100,000 (Kurtzke, 1980) and RR of 2.7, the 40-year added risk in workers, if real, might not reach the 1/1,000 benchmark, but would exceed the 1/100,000 environmental *de minimis* bench mark 85	(I1) Could be of environmental regulatory interest but might be considered *de minimis* from an occupational regulatory point of view.

TABLE 15.4.7

EVIDENCE FOR RACIAL OR CLASS DIFFERENCES IN EXPOSURE OR VULNERABILITY	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
No evidentiary base.	None.

TABLE 15.4.8

ROOM FOR IMPROVEMENT IN QUALITY OR SIZE IN BEST EXISTING STUDIES	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) There are no known confounders that were not dealt with or are credible alternative explanations in the cohort studies. They are sophisticated occupational studies and they agree with the case-control studies. (C2) The case-control studies leave a lot to be desired. The cohort studies are sophisticated and of good quality. Future study could explicitly deal with shocks and trauma and their association with EMF exposure and with a more modern approach to the histopathology of major and minor shocks.	(I1) While ALS is so rare that it is probably a *de minimis* risk from a regulatory point of view, a JEM exposure study could address the shock and contact-current hypotheses for this and other diseases. A mechanistic understanding of this association might be relevant to the association with other diseases.

TABLE 15.4.9

NEW STUDIES IN PIPELINE AND ABILITY TO CHANGE ASSESSMENT	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) A population case-control study by Nelson et al. will be looking at electric shocks but not EMFs per se. (C2) An incidence study of ALS and EMFs by Johansen is pending.	(I1) Not likely to change assessment.

TABLE 15.4.10

HOW LIKELY IS IT THAT FURTHER STUDIES COULD RESOLVE CONTROVERSIES?	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) A better JEM exposure study in electrical workers and in the general population could address the hypothesis that contact currents or small shocks are correlated with measured magnetic fields. This could lead to reanalysis of other studies and suggest exposure conditions for experimental studies. The association between EMFs and ALS is unlikely to be explained in one or two iterations of study.	(I1) Results of initial research would be needed to anticipate progress. Current assessment likely to remain for a decade at least.

15.5 CONCLUSIONS ON POLICY-RELEVANT SCIENTIFIC ISSUES

15.5.1 DOSE RESPONSE

Something about electrical occupations and aspects of those occupations that are associated with magnetic fields is associated with ALS. Shocks have been proposed as an explanation, and contact currents could also be invoked although there is no direct evidentiary basis for associating shocks, contact currents, and magnetic fields. Other aspects or non-TWA summary exposure metrics have not be invoked as an explanation. Decades of exposure with long induction period may be important. The evidentiary base is not present to discuss thresholds or plateaus, or biological windows of vulnerability or social or ethnic vulnerability or exposure.

15.5.2 RESEARCH POLICY

ALS is a rare disease and an association, if real, might not translate into an absolute risk which was above *de minimis* bench marks for occupational exposures. A job exposure matrix examining shocks, contact currents, and electric and magnetic fields with various summary exposure metrics might help resolve the shock vs. magnetic field explanations for ALS, if applied to the existing data bases. Clarity in this rare disease might have implications for more common diseases associated with EMF exposures.